Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May. 44 p. (Technology appraisal guidance; no. 284).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Please note that the National Institute for Health and Care Excellence (NICE) can only issue guidance on any drug within the terms of its marketing authorisation. Consequently, bevacizumab for first-line treatment of advanced ovarian cancer has only been appraised at its licensed dose of 15 mg/kg body weight.

- Bevacizumab in combination with paclitaxel and carboplatin is not recommended for first-line treatment of advanced ovarian cancer (International Federation of Gynaecology and Obstetrics [FIGO] stages IIIB, IIIC and IV epithelial ovarian, fallopian tube or primary peritoneal cancer).
- People currently receiving bevacizumab for first-line treatment of advanced ovarian cancer should be able to continue treatment until they and their clinicians consider it appropriate to stop.

Clinical Algorithm(s)

This guidance has been incorporated into a NICE Pathway for ovarian cancer, available from the National Institute for Health and Care Excellence (NICE) Web site .

Scope

Disease/Condition(s)

Advanced ovarian cancer (International Federation of Gynaecology and Obstetrics [FIGO] stages IIIB, IIIC and IV epithelial ovarian, fallopian tube or primary peritoneal cancer)

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Internal Medicine

Obstetrics and Gynecology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer

Target Population

Women with advanced (stage III or IV) ovarian cancer

Interventions and Practices Considered

Bevacizumab in combination with paclitaxel and carboplatin as first-line treatment (not recommended)

Major Outcomes Considered

- Clinical Effectiveness
  - Progression-free survival (PFS)
  - Overall survival (OS)
  - Objective response rate (ORR)
  - Adverse events (AEs)
  - Health-related quality of life (HRQoL)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Manufacturer's Search Strategy

The manufacturer's literature searches were checked by an information specialist. Overall, the searches are adequately documented by the manufacturer, with satisfactory database selection. The search strategy comprises the use of free text and index terms, appropriately combined. There were a few minor inconsistencies and errors, however not deemed significant enough to miss vital evidence. Differing host systems and syntax employed between the ERG and manufacturer dictates that the searches could not be exactly replicated. A suitable selection of conferences were cited as searched by the manufacturer both electronically and hand-searched. The ERG information specialist undertook some additional searches as follows: a fuller randomised controlled trial (RCT) filter search was applied to Medline and Embase. On-going trials searches were undertaken on the following clinical trials registries: UK Clinical Research Network (UKCRN) Study Portfolio, controlled-trials.com, clinical trials.gov and World Health Organisation International Clinical Trials Registry Platform (WHO ICTRP). The results were checked by an ERG researcher. No additional trials identified were relevant to the decision problem.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection

The manufacturer's submission (MS) clearly states the inclusion and exclusion criteria. The inclusion criteria reflect the final scope issued by NICE and the licensed indication; that is to include studies of patients with advanced ovarian cancer. However, the manufacturer did not specify dose of bevacizumab as an inclusion or exclusion criterion. This means that studies did not have to use the licensed dosage of bevacizumab (15 mg/kg) to be included in the review. Therefore, the inclusion criteria are wider than the scope and the licensed indication.

Study quality and setting were not stated as inclusion or exclusion criteria, and this reflects the final scope. Separate sets of criteria were used to assess RCT and non-RCT studies identified from the searches for inclusion. In the RCT inclusion and exclusion criteria, the only study design limitations were that phase I studies, non-RCT studies and reviews were excluded. In the non-RCT inclusion and exclusion criteria, studies that included fewer than 200 patients and RCT studies were excluded. The manufacturer does not provide a justification for excluding non-RCT studies with fewer than 200 patients, but they are transparent about which studies were excluded for this reason (these are listed in MS) and the ERG agrees that it is reasonable to exclude these studies. Issues of bias and study quality are not considered at the searching, screening or selection stages of the review, but the manufacturer provides a critical appraisal of the included studies.

The MS includes a flow diagram that shows the number of publications identified through the database searches and the number of publications included and excluded at each stage of the review. Reasons for excluding studies at the full publication review stage, along with the number excluded for each reason, are detailed in the diagram. Additionally, the manufacturer has provided lists of the RCT and non-RCT studies identified through the searches, and, where relevant, has recorded reasons for excluding publications in these lists (see Table 1 of the ERG report [see the "Availability of Companion Documents" field] for the list of included studies).

Economic Evaluation

Manufacturer's Review of Published Economic Evaluations

A systematic search of the literature was conducted by the manufacturer to identify economic evaluations of bevacizumab in advanced or metastatic ovarian cancer from a UK perspective using several health economic databases and medical databases. The inclusion and exclusion criteria for the systematic review are listed in the MS. The inclusion criteria state that cost-effectiveness studies of bevacizumab in advanced

ovarian cancer would be included.

Nine studies were identified and of these six studies were excluded, mainly as they were not cost-effectiveness studies. Three studies were included for full review.

Number of Source Documents

Clinical Effectiveness

One double-blind randomised controlled trial (RCT) and one randomised open-label trial were included.

Cost-Effectiveness

- Three studies were included for full review.
- The manufacturer submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of the Approach to Validity Assessment

The manufacturer's submission (MS) provides a quality assessment for both randomised controlled trials (RCTs). The quality assessment in the MS follows the NICE criteria and is appropriate. Table 2 of the ERG report shows the ERG independent assessment of study quality for the Gynaecologic Oncology Group (GOG)-0218 trial and the MS assessment. As this table shows, the ERG assessment partly agrees with that of the manufacturer.

Description and Critique of the Manufacturer's Approach to the Evidence Synthesis

The MS provides a narrative synthesis of the findings of the GOG-0218 trial. Some of the tabulated and narrative data in the MS differ to that reported in the trial paper for the overall survival (OS), health-related quality of life (HRQoL) analyses and subgroup analyses of progression-free survival (PFS). In terms of differences in the OS and HRQoL data reported in the MS and the trial paper, these do not change the interpretation of the data. The use of different alpha levels in the MS and trial paper for detecting statistically significant differences between the arms in the HRQoL analysis also does not affect the conclusions made about group differences for the HRQoL outcome.

In terms of the subgroup analyses of PFS, the analyses comparing the pooled bevacizumab-containing arms with the carboplatin, paclitaxel and placebo (CPP) arm are not comparable to the subgroup analyses reported in the original trial paper as in the paper the bevacizumab-containing arms were not pooled. The ERG notes that when the bevacizumab-containing arms were pooled, they generally showed favourable effects over

the CPP arm across subgroups; however, in the original paper, the subgroup analyses showed that while the CPB15+ arm (same standard chemotherapy as the CPP group, plus bevacizumab [15 mg/kg] for cycles 2 to 22) was generally superior in effectiveness across subgroups to the CPP arm, the CPB15 arm (same standard chemotherapy as the CPP group, plus bevacizumab (15 mg/kg) for cycles 2 to 6 and placebo as monotherapy for cycles 7 to 22) was not. The data for the subgroup analysis of PFS by disease stage and debulking status reported in the MS for each of the three arms differ to that reported in the trial paper, but the differences are minor and do not affect the interpretation of the data.

A meta-analysis of the GOG-0218 and ICON7 trials is not provided. The MS states that this is because the trials are not comparable in terms of treatment dose and duration and patient population. The ERG agrees with this decision.

Summary Statement of Manufacturer's Approach

See Table 4 of the ERG report for quality assessment of MS review.

The systematic review is of reasonable quality according to Centre for Reviews and Dissemination (CRD) criteria and the submitted evidence reflects the decision problem defined in the MS although no details are given for any of the processes used in the systematic review (i.e., whether assessment was by a single reviewer or independently by two reviewers).

Overall the risk of systematic error in the systematic review appears to be low. However, the systematic review was wider than the decision problem/scope and included an additional study which does not meet the population defined in the scope.

See Section 3 of the ERG report (see the "Availability of Companion Documents" field) for additional information on methods used to analyse clinical effectiveness.

Economic Evaluation

Manufacturer's Review of Published Economic Evaluations

Three studies were included for full review. The studies were quality assessed using the Drummond and Jefferson checklist (suggested by NICE). No interpretation or conclusions of this quality assessment were provided in the MS. Results were presented from the three studies but no discussion or conclusions were given on these results by the manufacturer. The ERG suggests that the review of the published economic evaluations could have been more informative by comparing and discussing the alternative model structures and the corresponding differences in model results from that developed by the manufacturer.

Critical Appraisal of the Manufacturer's Submitted Economic Evaluation

The ERG has considered the methods applied in the economic evaluation in the context of the critical appraisal questions listed in Table 10 of the ERG report (see the "Availability of Companion Documents" field), drawn from common checklists for economic evaluation methods (e.g., Drummond and colleagues). The critical appraisal checklist indicates that overall the manufacturer follows recommended methodological guidelines, with the exception of the time horizon, where a 10-year time horizon has been used, rather than a lifetime horizon.

NICE Reference Case

The NICE reference case requirements have also been considered for critical appraisal of the submitted economic evaluation (see Table 11 of the ERG report). The MS analysis follows the NICE reference case.

Modelling Approach/Model Structure

The MS cost-effectiveness analysis uses a 3-state semi-Markov model to estimate the cost-effectiveness of bevacizumab with health states consisting of PFS, Progression and Death. The model was developed in Microsoft Excel.

The perspective of the model is the UK National Health Service Personal Social Services (NHS PSS) and results are presented as the incremental cost per quality-adjusted life years (QALY) gained. The model adopted a time horizon of ten years with a cycle length of 1 week. The model costs and outcomes were discounted at 3.5% per annum. The MS justified the time horizon by stating that this is the duration of reliable long term survival in the target cohort. The ERG notes that after ten years about 10% of patients are still alive in the model and therefore considers that a longer time horizon should have been adopted.

In the model, all patients start in the PFS state. Patients move to the progression state according to the PFS trial data from GOG-0218 until 28 months, after which PFS is represented by a log logistic parametric function. After disease progression, patients may progress to death according to a constant probability. The model then allocates health state utility values to patients in the PFS and progression health states.

The MS describes the following structural assumptions: the base case models assumed that no vial sharing was permitted for patients receiving

bevacizumab (although this was tested in the sensitivity analysis) and adverse effects (AEs) requiring treatment were assumed to occur in the first week of the model. The ERG notes that bevacizumab is not administered until cycle two, whilst the model includes these AEs during the first cycle. Although this is unlikely to be consistent with clinical practice, the ERG considers that this assumption would have a negligible effect on the model results.

Consistency/Model Validation

Internal Consistency

The economic model was developed in Microsoft Excel, with two alternative versions submitted for the analyses relating to the GOG-0218 and ICON7 RCTs. Random checking of the model has been done for some of the key equations in the model. The ERG has not undertaken a comprehensive check of all cells in the model. The model was checked to see if results were in the expected directions and had expected magnitude for changes to the model input parameters. The electronic model is fully executable, and inputs changed on the 'Model Inputs' worksheet produce changes in the deterministic results in the 'Results Table' worksheet. These can be used to replicate the results presented in the MS and the deterministic sensitivity analyses for the base case model, as reported in MS. The ERG views the model as a reasonable approach to modelling the cost effectiveness of bevacizumab and from random checking the 'wiring' of the model appears to be accurate.

External Consistency

The MS states that the results from the manufacturer's model are broadly consistent with the published literature found in their review of cost-effectiveness studies, with the caveat that the published studies were for non-UK based healthcare systems.

The OS estimates from the model were compared in the MS to estimates from an external source using ovarian cancer patients with similar disease severity and surgical outcome. The MS reports that the results from the model overestimate the survival of patients receiving chemotherapy after approximately 30 months.

See Section 4 of the ERG report (see the "Availability of Companion Documents" field) for more information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions on the Manufacturer's Economic Model

Availability and Nature of Evidence

The manufacturer submitted a 3-state semi-Markov model with health states consisting of progression-free survival (PFS), progressed disease and death. Data from Gynaecologic Oncology Group (GOG)-0218 were used to inform model inputs for dosing, survival and safety. Both the intervention and comparator in the model were used in accordance with their marketing authorisations.

The Committee concluded that the manufacturer's model adhered to the National Institute for Health and Care Excellence (NICE) reference case for economic analysis and was acceptable for assessing the cost-effectiveness of bevacizumab plus paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee considered the model inputs, including clinical effectiveness, patient outcomes, resource use and costs, and concluded that they were reasonable.

The Committee understood the Evidence Review Group (ERG) concerns about the treatment duration of 12 months instead of the 15 months specified in the marketing authorisation and a time horizon of 10 years. The ERG did not consider this time horizon to be long enough, although the Committee heard from the clinical specialists that 10 years was probably appropriate because only a very small number of patients are likely to survive beyond 10 years.

The Committee noted the manufacturer's response to the appraisal consultation document, which attempted to adjust for crossover in the GOG-0218 study by applying the overall survival curves estimated for the control and treatment arms in the expanded high-risk subgroup from the ICON7 study, rather than using post-progression survival data from the GOG-0218 study. The Committee agreed that this was an unconventional approach that lacked credibility because of the significant differences identified between the 2 studies.

Incorporation of Health-Related Quality-of-Life Benefits and Utility Values/Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee noted that the EQ-5D utilities from the expanded high-risk subgroup of ICON7 were used in the model and that the same utilities were assumed in both arms of the model.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost-Effective?

No. The Committee agreed that the range of incremental cost-effectiveness ratios (ICERs) obtained from the cost-effectiveness model of bevacizumab plus paclitaxel and carboplatin were outside the range normally considered as a cost-effective use of National Health Service (NHS) resources. It therefore concluded that bevacizumab within its marketing authorisation (that is, at a dose of 15 mg/kg), plus paclitaxel and carboplatin, would not be a cost-effective use of NHS resources for first-line treatment of advanced ovarian cancer compared with paclitaxel and carboplatin alone.

What Are the Key Drivers of Cost-Effectiveness?

The manufacturer's deterministic sensitivity analysis for GOG-0218 suggested that the cost-effectiveness results are influenced by the parametric functions used for the PFS extrapolation and the time horizon used in the model. The manufacturer's scenario analyses identified the key drivers of the cost-effectiveness results as the dose and duration of bevacizumab treatment.

Most Likely Cost-Effectiveness Estimate (Given as an ICER)

The Committee noted that the manufacturer's base-case ICER was approximately £144,000 per quality-adjusted life-year (QALY) gained. The Committee considered the ERG's exploratory analyses, which examined the changes in the ICER with a treatment duration of 15 months or a time horizon of 25 years or both, and gave a range of ICERs from £128,000 to £161,000 per QALY gained.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of bevacizumab and a review of this submission by the Evidence Review Group. For clinical effectiveness, one randomised controlled trial (RCT) was the main source of evidence. For cost-effectiveness, the manufacturer's model and 3 published economic evaluations were considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate recommendation for the use of bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer

Potential Harms

The summary of product characteristics lists the following adverse reactions that may be associated with bevacizumab treatment: gastrointestinal perforations, fistulae, wound healing complications, hypertension, proteinuria, arterial and venous thromboembolism, haemorrhage, pulmonary haemorrhage or haemoptysis, congestive heart failure, posterior reversible encephalopathy syndrome, hypersensitivity or infusion reactions, osteonecrosis of the jaw, ovarian failure and neutropenia.

For full details of adverse reactions and contraindications, see the summary of product characteristics available at http://emc.medicines.org.uk/ .

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed a tool to help organisations put this guidance into practice. This tool is available from the NICE Web site : a costing statement explaining the resource impact of this guidance.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May. 44 p. (Technology appraisal guidance; no. 284).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 May

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May 3 p. (Technology appraisal 284). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Cooper K, Pickett K, Frampton GK, Copley V, Bryant J. Bevacizumab in combination with carboplatin and paclitaxel for the first-line treatment of ovarian cancer. A single technology appraisal. London (UK): Southampton Health Technology Assessments Centre (SHTAC); 2012. 60 p. Electronic copies: Available from the NICE Web site .
- Ovarian cancer overview. NICE pathway. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May. (Technology appraisal 284). Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Bevacizumab with paclitaxel and carboplatin as first-line treatment for advanced ovarian cancer. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 May. 6 p. (Technology appraisal 284). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on August 27, 2013.

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